TITLE

METHODS OF ANORECTAL MANOMETRY VARY WIDELY IN CLINICAL PRACTICE: RESULTS FROM AN INTERNATIONAL SURVEY

RUNNING TITLE

ANORECTAL MANOMETRY PRACTICE SURVEY

AUTHORSHIP

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ABSTRACT

Background

Anorectal manometry (ARM) is the most commonly performed investigation for assessment of anorectal dysfunction. Its use is supported by expert consensus documents and international guidelines. Variation in technology, data acquisition and analysis affect results and clinical interpretation. This study examined variation in ARM between institutions to establish the status of in current practice.

Methods

A 50-item web-based questionnaire assessing analysis and interpretation of ARM was distributed by the International Anorectal Physiology Working Group (IAPWG) via societies representing practitioners that perform ARM. Study methodology and performance characteristics between institutions were compared.

Key results

One-hundred and seven complete responses were included from 30 countries. Seventy-nine (74%) institutions performed at least 2 studies per week. Forty-nine centres (47%) applied conventional ARM (≤8 pressure sensors) and 57 (53%) high-resolution ARM (HR-ARM). Specialist centres were most likely to use HR-ARM compared to regional hospitals and office based practice (63% *vs.* 37%). Most conventional ARM systems used water-perfused technology (34/49); solid-state hardware was more frequently used in centres performing HR-ARM (44/57). All centres evaluated rest and squeeze. There was marked variation in the methods used to report results of maneuvers. No two centres had identical protocols for patient

preparation, setup, study and data interpretation and no centre fully complied with published guidelines.

Conclusions and Inferences

There is significant discrepancy in methods for data acquisition, analysis and interpretation of ARM. This is likely to impact clinical interpretation, transfer of data between institutions and research collaboration. There is a need for expert international co-operation to standardize ARM.

KEYWORDS

Anal manometry

Anorectal manometry

High-resolution anorectal manometry

Anorectal physiology

Anorectal dysfunction

Faecal / fecal incontinence

Constipation

KEYPOINTS

- There is marked variation in technology employed, data acquisition, analysis and reporting of ARM results between institutions.
- More than half of the centres surveyed use high-resolution ARM for the performance of anorectal manometry. High-resolution technology was utilized most often in specialist centres with high throughput.
- None of the centres surveyed complied fully with the widely cited guidelines for ‘minimum standards’ of anorectal manometry.

ABBREVIATIONS

AGIP	Association of GI Physiologists
ANGMA	Australasian Neurogastroenterology and Motility Association
ANMA	Asian Neurogastroenterology and Motility Association
ANMS	American Neurogastroenterology and Motility Society
ARM	Anorectal manometry
ENMS	European Neurogastroenterology and Motility Society
HR-ARM	High-resolution anorectal manometry
IAPWG	International Anorectal Physiology Working Group
RAIR	Rectoanal inhibitory reflex
USA	United States of America
UK	United Kingdom

INTRODUCTION

Several investigations are available for the assessment of anorectal structure and function in patients who present with intractable symptoms of anorectal dysfunction, characterised by faecal incontinence and / or disordered evacuation (1-3). Anorectal manometry (ARM) is the best-established technique available to detect abnormalities of sphincter function and / or recto-anal co-ordination, which may important causes of such symptoms (2, 4, 5).

ARM consists of a series of pressure measurements that assess: (i) involuntary function of the anal canal during rest, (ii) voluntary function during squeeze, (iii) reflex recto-anal co-ordination during rectal stimulation, and (iv) voluntary rectoanal co-ordination during simulated defecation ('push') (3, 4). ARM may also incorporate an assessment of rectal sensation (4).

Review articles that describe the ARM technique (3, 4, 6-9) reveal that variations of study protocol impact the results of this investigation (4, 10-13). This limits clinical interpretation, transfer of data between institutions and research collaboration. For these reasons, several position statements and working party reports have provided guidance on technique for data acquisition, analysis and reporting (1, 4, 8, 14). Nevertheless, several manometry systems are commercially available and, although evidence is lacking, it is widely presumed that there is important variation in practices between institutions (15-21).

The advent of high-resolution ARM (HR-ARM) has brought with it a new dimension of data capture and visualization (colour-contour topographical plots), and has the

potential to revolutionize appreciation of anorectal function (22-24). Unfortunately, this advancement has added a further element of variability in practice; unless efforts are made early to reach consensus on test performance, this technique may fall victim to the same pitfalls that have bedeviled other investigations in the field.

To address these knowledge gaps, and to bring consensus, an expert group (the International Anorectal Physiology Working Group [IAPWG]) was convened to develop and promote internationally accepted standards for the clinical measurement of anorectal physiology, with a particular focus on HR-ARM. As a first step, and to better understand the status of current practice, the group conducted this study to examine ARM practice in different settings and countries. This work tests the hypothesis that there is important variation in ARM practice. The objectives are to inform and facilitate the development of internationally agreed standard operating procedures for data acquisition and analysis.

METHODS

Questionnaire structure

A questionnaire examining features of ARM practice was developed using a web-based survey and data collection tool (www.qualitrics.com, Utah, USA). The questionnaire is available in Supplementary material 1. Existing guidelines (2, 4, 8) were used to structure the questionnaire to explore the following areas of interest:

1) department setup / centre activity;
2) study indications;
3) manometry technique and equipment;
4) study protocol;
5) data analysis and reporting;
6) additional investigations.

'Department setup / centre activity' explored centre location / specialism and volume of activity performed. 'Study indications' allowed respondents to choose common reasons for test performance (e.g. faecal incontinence, constipation etc.). 'Manometry technique and equipment' examined the use of conventional ARM and / or HR-ARM, and detailed the equipment used. 'Study protocol' comprised a series of questions related to common manoeuvres performed to assess rest, squeeze, prolonged squeeze, cough, push (simulated defecation) and the recto-anal inhibitory reflex (RAIR). 'Data analysis and reporting' explored reporting of test results. 'Additional investigations' allowed the respondent to list tests used to complement ARM in the assessment of symptoms of disordered defecation.

Data were collected in the form of single or compound answer multiple-choice questions for nominal data, slider bar questions for continuous numerical data and

open-ended text boxes for descriptive exploration of complex practices. In particular, questions exploring measurement parameters were constructed using a `select all that apply` approach.

Prior to launch, the questionnaire was piloted by 10 UK institutions to test usability, understanding, clarity and question flow.

Questionnaire distribution

Practitioners (clinicians, nurse specialists, and physiologists) who regularly practice ARM were identified and contacted by email via advocates from the following national and international societies with an involvement in colorectal function testing: the Association of GI Physiologists (AGIP) of the British Society of Gastroenterology, the American Neurogastroenterology and Motility Society (ANMS), the Australasian Neurogastroenterology and Motility Association (ANGMA), the Asian Neurogastroenterology and Motility Association (ANMA), and the European Neurogastroenterology and Motility Society (ENMS). In addition, invitations were sent to those attending the 2013 Pelvic Floor Society Annual Meeting, and through clinicians involved in the International Anorectal Physiology Working Group (IAPWG) to their own clinical contacts with an interest in the field of ARM.

No incentive was utilised to increase response rate. The survey was distributed between September 2013 and July 2015. Responses not completed within 7 days of commencement were discarded.

This work was undertaken with the endorsement of all societies involved. Data were collected and held within the requirements of the Data Protection Act. The study did not use clinical data and did not require or seek specific ethical approval.

Statistical analysis

Data were analyzed quantitatively using number of observations and proportions. For centre activity comparisons, ‘high’ volume centres were defined as those performing ≥10 studies per week and ‘low’ volume centres were defined as those performing ≤2 studies per week.

Analyses were performed using a commercially available software package (SPSS Statistics Version 20: IBM, New York, USA). A P value of <0.05 was considered statistically significant.

RESULTS

Questionnaire responses

One hundred and nine responses were completed from 125 surveys started (87.2% completion rate). Two duplicate responses from individuals within the same centre were received. In each case, the second response was discarded. This left 107 complete surveys available for analysis. Responses were received from 30 countries as detailed in Table 1.

Centre activity

Seventy-nine centres (74%) reported performing more than 2 studies per week with most reporting activity of between 2 – 10 studies per week (52%). Particularly high volume activity (≥20 studies per week) was reported by 8 (8%) centres and low volume activity by 13 centres (12%).

Forty-nine respondents (46%) described their centre as being within a specialist hospital, 34 (32%) within a general hospital and 24 (22%) within a private hospital or other institution.

Study indications

Ninety-one respondents (85%) reported that ARM was ‘always’ performed for assessment of fecal incontinence, with the remaining 16 (15%) reporting that ARM was ‘sometimes’ performed for this indication. Eighty-six respondents (80%) reported ‘always’ performing ARM for assessment of constipation, with the remaining 21 (20%) reporting ‘sometimes’. ARM was less often performed for anal pain (10% never, 65%

sometimes, 25% always) and for abdominal pain / bloating (59% never, 34% sometimes, 7% always).

Manometry technique and equipment

Fifty-seven (53%) centres reported using HR-ARM. Forty-nine utilised conventional ARM (47%). One centre reported using both HR-ARM and conventional ARM.

Of the 49 centres performing conventional ARM, 34 (69%) reported using water-perfused technology. The remaining 15 (31%) use a solid-state catheter. Water-perfused systems were far less common in those centres performing HR-ARM, with only 13 (23%) using this technology and the remaining 44 (77%) institutions using a solid state catheter.

There was marked variation in catheter diameter, sensor number and sensor / port configuration between centres. Catheter diameter varied between 8 – 22F for both water-perfused and solid-state systems. These data are summarized in Tables 2a and 2b.

Study protocol and measurement reporting

Manoeuvres performed

The only tests consistently performed by all centres during ARM were the rest and squeeze manoeuvers. For the other manoeuvers, 87 (81%) reported performing prolonged squeeze, 89 (83%) cough, 89 (83%) push (simulated defecation) and 103 (96%) RAIR.

Rest

The time period most frequently used to record anal resting pressure was 1 minute (76%). The method of reporting most frequently used was ‘mean pressure over the whole anal canal length’ (55%). These data are further described in Figure 1.

As questions were designed as ‘select all that apply’, it was possible to assess the combination of measurement parameters utilised by each institution. This analysis demonstrated that there were 16 combinations of ways in which rest data were quantitatively reported. The three most common reporting methods were ‘mean pressure over the whole anal canal length’ alone (29%), ‘mean pressure at different levels of the anal canal’ alone (15%), and ‘mean pressure over the whole anal canal length’ together with ‘maximum pressure over the whole anal canal’ (14%).

Squeeze

During assessment of squeeze, 69 (65%) centres routinely asked subjects to squeeze for a predefined length of time, with 37 (35%) centres allowing subjects to squeeze for ‘as long as they were able’. One centre (1%) failed to give valid information on squeeze characteristics.

Of those asking subjects to squeeze for a predefined length of time, the most commonly reported squeeze *duration* was 5 seconds (18% of respondents) however there was very little consistency between centres, and 26 (24%) centres reported that requested *short* squeeze duration was >15 seconds. These data are presented in Figure 2a. There was also marked discrepancy between centres in the *number* of

squeeze performed, which varied between 1 and 10**.** These data are presented in Figure 3a.

As with parameters of resting anal pressure, there was marked variation in the methods used to report results. The two most common squeeze parameters reported were ‘maximum incremental squeeze pressure’ (56%) and ‘maximum absolute squeeze pressure’ (51%). These data are further explored in Figure 1.

There were 18 combinations of ways in which squeeze data were quantitatively reported. The three most common reporting methods were ‘maximum incremental squeeze pressure’ alone (21%), ‘maximum absolute squeeze pressure’ alone (13%), and ‘maximum incremental squeeze pressure’ together with ‘maximum absolute squeeze pressure’ (12%).

Prolonged squeeze

Similar to the results found with squeeze, there was marked variation in the performance and reporting of *prolonged* squeeze. The *duration* of prolonged squeeze most frequently reported was 20s or 30s (25% for both) however the reported duration ranged up to 60 seconds. These data are shown in Figure 2b. There was similar discrepancy in the *number* of squeezes performed, which varied between 0 and 10. These data are shown in Figure 3b.

There was particular variation in results reporting of this manoeuvre. The most common parameters reported for prolonged squeeze were ‘duration of squeeze above 50% maximum pressure’ (47%). These data are shown in Figure 1.

There were 43 combinations of ways in which prolonged squeeze data were quantitatively reported. The two most common reporting methods were ‘duration of squeeze above 50% maximum pressure’ alone (20%) and ‘maximum absolute pressure’ alone (10%).

Cough

As previously, there was marked variation in the performance and reporting of the cough manoeuvre. The *number* of cough manoeuvres performed varied between 1 and 10.

Notably, 36 centres (40%) reported that they do not use quantitative values to describe results and that instead qualitative assessment of muscle recruitment is utilised. Of those using quantitative measures, the most common metric used was ‘maximum anal pressure during cough’, which was reported by 28 (31%) of these institutions. These data are shown in Figure 1.

There were 12 combinations of ways in which cough data were quantitatively reported. The two most common combinations were the use of ‘maximum anal pressure’ alone (12%) and ‘maximum rectal pressure during cough’ together with ‘maximum anal pressure during cough’ (10%).

Push (simulated defecation)

As with other manoeuvres, there were notable dissimilarities in test performance and results reporting of push between centres. Of the 89 institutions that reported

performing push, the majority (91%) performed this test with the subject in the left lateral position. Interestingly, 6 centres (7%) performed the study in both in the left lateral *and* the sitting position, 1 centre (1%) performed studies in the left lateral *and* supine position and 1 centre (1%) performed studies in the left lateral, supine *and* the sitting position (Table 3). As seen previously for other manoeuvres, there was particular variability in the *number* of push manoeuvres performed, which varied between 1 and 10. These data are shown in Figure 3 c.

For the performance of this test, 65 (73%) centres reported the use of a rectal balloon associated with the manometry catheter. Nine centres (14% of those using a balloon) routinely fill the balloon to the subjects' first sensory volume, 9 (14%) to the subjects' defaecatory desire volume and 45 (69%) to a pre-defined fixed amount. Two (3%) institutions did not provide information about balloon filling. For those reporting the use of a predefined amount for balloon inflation, the most commonly used amount of air was 50 ml, which was reported by 27 (64%) of these institutions.

For reporting of the push manoeuvre, in the context of a 'select all that apply' question format, 21 (24%) centres report push qualitatively from colour contour / line traces and 47 (53%) provide quantitative reports using either in-built analysis software or by deriving values manually from line traces. Twelve (13%) stated that they only report practitioner evaluated visualisation of appropriate muscle recruitment / co-ordination. Twenty-nine centres (33%) did not give information on how push was manometrically reported.

RAIR

Overall 103 centres routinely perform RAIR assessment. Of these, the majority perform one RAIR during each study (39%). Again however, there was great variability, with 2 centres (2%) reporting that they routinely perform 10 RAIRs as part of their standard clinical protocol. These data are shown in Figure 3d.

Thirty-six centres (36%) report provoking RAIR by incremental inflation of a rectal balloon by fixed volumes of air, and 17 (17%) with only a *single* fixed volume of air. Forty-eight (47%) did not provide information about the inflation method for the provocation of RAIR.

Thirty (29%) centres reported measuring the RAIR quantitatively, 37 (36%) qualitatively (as present / absent), and 34 (33%) both quantitatively and qualitatively. Six (6%) centres did not provide information of the method used for RAIR reporting.

Additional investigations

No centre reported performing ARM in isolation. All centres reported that they perform at least one other complimentary test of anorectal structure / function (Table 4).

Comparison between centres using conventional ARM *or* HR-ARM

Some differences were seen in demographics and practices when comparing those centres performing conventional ARM versus those performing newer HR-ARM. Within this survey sample, HR-ARM is more frequently utilised by specialist and private hospitals (43/67 [64%] *vs.* 36% performing conventional ARM), whereas conventional ARM is more frequently performed in general hospitals (23/34 [68%] *vs.*

11/34 [32%] performing HR-ARM). Activity between conventional ARM and HR-ARM performing centres was similar, with 6 (6/49 [12%]) conventional ARM *vs.* 7 (7/57 [12%]) HR-ARM centres reporting low volume activity and 6 (6/49 [12%]) conventional ARM vs. 9 (9/57 [16%]) HR-ARM centres reporting high volume activity.

HR-ARM was more commonly reported amongst centres from North and South America (used by 27/36 [75%]). By contrast, it appears that conventional ARM remains popular in the rest of the world with 8 (8/14 [57%]) centres from Asia, the Middle East and Australia and 35 (35/57 [61%]) of European centres continuing to use this technique.

Despite difficulties in interpreting the widespread variation in methods used to report manometric findings, there was an apparent higher frequency of more integrative or qualitative measures of anorectal function used by centres with HR-ARM. Pertinent examples include:

- rest - ‘mean pressure over the anal canal’ reported by 17 (17/49 [35%]) conventional ARM centres *vs*. 42 (42/57 [74%]) HR-ARM centres;
- push - ‘qualitative reporting of anorectal co-ordination’ was utilized by 3 (3/49 [6%]) conventional ARM centres *vs*. 18 (18/57 [32%]) HR-ARM centres;
- cough - ‘qualitative visualisation of muscle recruitment / co-ordination’ was reported by 6 (6/49 [12%]) conventional ARM centres *vs*. 20 (20/57 [35%]) HR-ARM centres.

Compliance with guidelines

Results were compared with the protocol outlined in the most widely accepted guideline for ARM (4). This manuscript recommends a minimum 6-sensor catheter with performance of rest, squeeze, cough, push and RAIR maneuvers and suggests reporting of the following basic parameters: `maximum anal resting pressure at intervals within the anal canal ', 'maximum anal squeeze pressure', 'maximum sustained squeeze pressure', 'squeeze duration', 'rectoanal pressure difference during cough', 'residual anal pressure during push' and 'combined qualitative / quantitative reporting of the RAIR'. Only three centers complied with the suggested performance protocol. None of the 107 centers surveyed complied with both the recommended protocol and method for results reporting. In addition, no two centers reported identical protocol and analysis techniques.

DISCUSSION

This study confirms the long held impression that striking variation exists in the current practice of ARM. Differences between institutions exist in study indications, equipment used, manometry technique, data acquisition, analysis and reporting. No centre responding to this survey fully complies with previously published and widely cited 'minimum standards' for ARM (4). In particular, there is dissimilarity in the parameters used to report results, a factor that makes accurate comparisons between institutions and further development of the technique challenging.

In an environment in which several commercial entities are developing and manufacturing diagnostic technologies, a degree of variation is inevitable and may be welcomed for the purposes of innovation. However, when such techniques are applied to clinical practice, nuance in equipment characteristics can have important effects on manometry measurements. This has been studied in both the upper and lower GI tract, and although most studies report good correlation between techniques, absolute values do significantly differ (12, 25-28). This represents a challenge to standardisation, as until robust evidence on actual differences in measurement and analysis exists, practitioners will continue to be driven by personal/institutional preference when choosing device and equipment specifications.

It is clear that the introduction of HR-ARM has brought with it further variability (9). This survey demonstrates that although conventional ARM is most commonly used in combination with water-perfused technology (69% of institutions surveyed), many of those with more novel HR-ARM systems have chosen to use solid-state hardware (77% institutions surveyed). The impact of these differences in hardware/software

combinations is yet to be quantified in the anorectum, however studies in the oesophagus indicate that the choice of technology and can impact diagnostic decision-making (29-32).

In addition, although (limited) normal values for different catheter types and populations exist (15, 33-36), a robust description of pathological measurements seen using HR-ARM is yet to be established. This is likely to explain our finding that, compared to those using conventional ARM, clinicians using modern HR-ARM equipment put more emphasis on qualitative descriptions of global anorectal function than quantitative pressure measurements. Data expression using the colour-contour display requires a illustrative approach, and in the oesophagus at least, this has been shown to significantly aid data interpretation and analysis (37).

Differences in practice were not limited to hardware/software combinations, but appeared to pervade all aspects regarding performance of the technique. The impact of variation in study protocol on ARM results and management of patients with anorectal disorders has not been robustly tested however, it has been shown that changes in patient position, doctor-patient interaction and data analysis all have important effects on anorectal measurements that can impact on clinical diagnosis (13, 38, 39).

A number of features found during investigation of study protocol invite discussion. Of particular interest was the finding that the majority of centres perform push in the left lateral position. Although sitting is clearly more physiological, only 8% of centres chose to investigate patients in this manner. It is often argued that testing in the left-lateral

position is one reason for the high rate of dyssynergia in both healthy and patient populations (40, 41) and investigation in the upright-seated position has been shown to influence rectal and anal pressure (42, 43). Certainly further exploration of the impact of patient position is warranted.

Another area for consideration is the near universal (96% of institutions surveyed) assessment of the RAIR. Although this is viewed as a useful screening test in paediatric populations (to exclude the presence of Hirschsprung disease) no formal evidence of the application of this test in adult populations exist (44, 45), especially as new diagnosis of this disorder in adults is exceptionally rare and usually made on clinical, radiological and histological grounds.

Additionally, despite a lack of evidence for its diagnostic utility (4, 8, 46), cough was performed by 83% of centres. The majority reported qualitative values and when quantitative values were reported there was significant variation in results reporting. The significant variation in results reporting between centres surveyed seem to indicate that the rationale for this test is poorly understood.

The finding of discordance in results reporting is particularly interesting. Although current guidelines recommend the utilisation of certain measures for resting and squeeze pressure (4, 8, 46) the diagnostic value of the different measures for discriminating health and disease states is limited (46, 47). This is likely in part to explain the finding that there were 16 combinations of ways in which rest, 18 combinations of ways in which squeeze and 43 combinations of ways in which prolonged squeeze data were quantitatively reported. This inconsistent use of

terminology and methods for data acquisition and analysis of ARM findings requires specific discussion because at the very least, such practice can cause confusion when communicating results between practitioners both in the clinical setting and also when published in the literature. This variability can be partly explained by the fact that there are few published studies that investigate the *comparative* utility of individual manometric measures. There is no evidence to date that demonstrates that one manometric measure conveys superior diagnostic information to another. In addition, although it is well accepted that sphincter pressures are lower in patients with faecal incontinence than in health (48-57) there is only limited evidence that the *degree* of functional abnormality of the sphincter is related to symptom severity or predictive of treatment success (57-61).

Guidelines for the diagnosis and management of anorectal disorders recommend more than one test to better characterize pathophysiology and guide treatment. (8, 62, 63). The findings of this study show, that the majority of centres surveyed do utilize allied tests such as balloon expulsion, rectal sensation testing and measurement of colonic transit for assessment of anorectal dysfunction. However information in the literature on agreement of adjunctive tests and their results with HR-ARM especially in the diagnosis of evacuation disorders is conflicting (64, 65). Up to this time point no studies have investigated the added diagnostic value of different adjunctive testing methods to allow the recommendation of standardized testing sequences of HR-ARM and adjunctive tests for faecal incontinence or evacuation disorders.

For this reason published guidelines have been generally based on expert experience and opinion rather than an objective comparison of the utility of different manometric measures or adjunctive tests (3). Indeed, this lack of consensus may be the reason

for the relatively slow adoption and rate of publication with HR-ARM compared to oesophageal HRM for which a well-established method and classification system exists (66).

The authors acknowledge a number of limitations within this study. The first is the method for identification of potential respondents. Efforts were made to identify as many centres as possible through interaction with the societies with an interest in investigation of anorectal function and contacts of the IAPWG. This convenience sample may not necessarily be representative of global practices as a whole, particularly as some centres (especially low volume centres which do not engage formally with the societies) may have been underrepresented in the sample. In particular, over 27% of responses were collected from British centres. Therefore, although responses have been collected from 6/7 continents of the world, it would be fair to suggest that results may not be a true reflection of global practices with some bias to practices within the UK and Europe. The second limitation is the likely survey nonresponse bias. As the survey was distributed by third-parties to mailing lists no data pertaining to response rate were collected. It is possible that these non-respondents differed in meaningful ways from those who completed the survey resulting in voluntary response bias.

Third are the limitations implicit in design of this pragmatic questionnaire. Due to the complexity of results recording, options for reporting of certain manometric measures and measures of centre activity had to be given as close ended, leading questions. This may have led to response bias due to the lack of study blinding and desire of the respondent to give a ‘correct’ response. Questions did not force a response, which led

to some missing data, particularly for cough and RAIR characteristics. Additionally, there was no data accuracy / question check in place. It is possible that inattention from respondents may have led to inaccurate responses. This may be an explanation for the finding that endurance squeeze duration in some centres was less than 10 seconds.

This study provides the first formal evidence of major discordance in international practices of anal manometry. It has demonstrated that methods of both data collection and results reporting are extremely variable and it appears that many centres are not following currently acknowledged best practice. This disparity is likely to be limiting the utility of this technique, preventing data comparison between institutions and may be impacting on clinical decision-making.

This study provides a basis for consensus generation in regards to manometric data acquisition and analysis of anorectal measurements akin to the Chicago process for assessment of oesophageal function (67). Such agreement on standard operating is urgently required to reduce undesirable variations in practice and ultimately, the formation of good clinical guidelines for anorectal manometry is likely to have a significant impact on both the clinical and research applications of this technique.

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REFERENCES

1. Barnett JL, Hasler WL, Camilleri M. American Gastroenterological Association medical position statement on anorectal testing techniques. American Gastroenterological Association. *Gastroenterology* 1999; **116**: 732-760.
2. Diamant NE, Kamm MA, Wald A, Whitehead WE. AGA technical review on anorectal testing techniques. *Gastroenterology* 1999; **116**: 735-760.
3. Scott SM, Gladman MA. Manometric, sensorimotor, and neurophysiologic evaluation of anorectal function. *Gastroenterol Clin North Am* 2008; **37**: 511-538, vii.
4. Rao SS, Azpiroz F, Diamant N, Enck P, Tougas G, Wald A. Minimum standards of anorectal manometry. *Neurogastroenterol Motil* 2002; **14**: 553-559.
5. Rao SS. Pathophysiology of adult fecal incontinence. *Gastroenterology* 2004; **126**: S14-22.
6. Felt-Bersma RJ, Meuwissen SG. Anal manometry. *Int J Colorectal Dis* 1990; **5**: 170-173.
7. Sun WM, Rao SS. Manometric assessment of anorectal function. *Gastroenterol Clin North Am* 2001; **30**: 15-32.
8. Azpiroz F, Enck P, Whitehead WE. Anorectal functional testing: review of collective experience. *Am J Gastroenterol* 2002; **97**: 232-240.
9. Lee TH, Bharucha AE. How to Perform and Interpret a High-resolution Anorectal Manometry Test. *Journal of neurogastroenterology and motility* 2016; **22**: 46-59.
10. Schouten WR, van Vroonhoven TJ. A simple method of anorectal manometry. *Dis Colon Rectum* 1983; **26**: 721-724.
11. Rao SS, Hatfield R, Soffer E, Rao S, Beaty J, Conklin JL. Manometric tests of anorectal function in healthy adults. *Am J Gastroenterol* 1999; **94**: 773-783.
12. Simpson RR, Kennedy ML, Nguyen MH, Dinning PG, Lubowski DZ. Anal manometry: a comparison of techniques. *Dis Colon Rectum* 2006; **49**: 1033-1038.
13. Heinrich H, Fruehauf H, Sauter M*, et al.* The effect of standard compared to enhanced instruction and verbal feedback on anorectal manometry measurements. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society* 2013; **25**: 230-237, e163.
14. Keighley MR, Henry MM, Bartolo DC, Mortensen NJ. Anorectal physiology measurement: report of a working party. *Br J Surg* 1989; **76**: 356-357.
15. Carrington EV, Brokjaer A, Craven H*, et al.* Traditional measures of normal anal sphincter function using high-resolution anorectal manometry (HRAM) in 115 healthy volunteers. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society* 2014; **26**: 625-635.
16. Carrington EV, Grossi U, Knowles CH, Scott SM. Normal values for high-resolution anorectal manometry: a time for consensus and collaboration. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society* 2014; **26**: 1356-1357.
17. Cali RL, Blatchford GJ, Perry RE, Pitsch RM, Thorson AG, Christensen MA. Normal variation in anorectal manometry. *Dis Colon Rectum* 1992; **35**: 1161-1164.
18. Chaliha C, Sultan AH, Emmanuel AV. Normal ranges for anorectal manometry and sensation in women of reproductive age. *Colorectal Dis* 2007; **9**: 839-844.
19. Gundling F, Seidl H, Scalercio N, Schmidt T, Schepp W, Pehl C. Influence of gender and age on anorectal function: normal values from anorectal manometry in a large caucasian population. *Digestion* 2010; **81**: 207-213.

718 20. Schuld J, Kollmar O, Schluter C, Schilling MK, Richter S. Normative values in
719 anorectal manometry using microtip technology: a cohort study in 172 subjects. *Int J*
720 *Colorectal Dis* 2012; **27**: 1199-1205.
721 21. Noelting J, Ratuapli SK, Bharucha AE, Harvey DM, Ravi K, Zinsmeister AR. Normal
722 values for high-resolution anorectal manometry in healthy women: effects of age and
723 significance of rectoanal gradient. *Am J Gastroenterol* 2012; **107**: 1530-1536.
724 22. Dinning PG, Carrington EV, Scott SM. The use of colonic and anorectal high-
725 resolution manometry and its place in clinical work and in research.
726 *Neurogastroenterology and motility : the official journal of the European Gastrointestinal*
727 *Motility Society* 2015; **27**: 1693-1708.
728 23. Clouse RE, Staiano A, Alrakawi A. Development of a topographic analysis system
729 for manometric studies in the gastrointestinal tract. *Gastrointest Endosc* 1998; **48**: 395-
730 401.
731 24. Dinning P, Carrington E, Scott SM. Colonic and anorectal motility testing in the
732 high-resolution era. *Curr Opin Gastroenterol* 2016; **32**: 44-48.
733 25. Jones MP, Post J, Crowell MD. High-resolution manometry in the evaluation of
734 anorectal disorders: a simultaneous comparison with water-perfused manometry. *The*
735 *American journal of gastroenterology* 2007; **102**: 850-855.
736 26. Fang JC, Hilden K, Tuteja AK, Peterson KA. Comparison of air-coupled balloon
737 esophageal and anorectal manometry catheters with solid-state esophageal manometry
738 and water-perfused anorectal manometry catheters. *Dig Dis Sci* 2004; **49**: 1657-1663.
739 27. Vitton V, Ben Hadj Amor W, Baumstarck K, Grimaud JC, Bouvier M. Water-Perfused
740 Manometry Versus 3-D High Resolution Manometry: A Comparative Study On A Large
741 Patient Population With Ano-Rectal Disorders. *Colorectal Dis* 2013.
742 28. Kang HR, Lee JE, Lee JS*, et al.* Comparison of High-resolution Anorectal Manometry
743 With Water-perfused Anorectal Manometry. *Journal of neurogastroenterology and*
744 *motility* 2015; **21**: 126-132.
745 29. Fox MR, Pandolfino JE, Sweis R*, et al.* Inter-observer agreement for diagnostic
746 classification of esophageal motility disorders defined in high-resolution manometry. *Dis*
747 *Esophagus* 2015; **28**: 711-719.
748 30. Carlson DA, Ravi K, Kahrilas PJ*, et al.* Diagnosis of esophageal motility disorders:
749 esophageal pressure topography vs. conventional line tracing. *Am J Gastroenterol* 2015;
750 **110**: 967-977; quiz 978.
751 31. Roman S, Bruley des Varannes S, Pouderoux P*, et al.* Ambulatory 24-h oesophageal
752 impedance-pH recordings: reliability of automatic analysis for gastro-oesophageal reflux
753 assessment. *Neurogastroenterol Motil* 2006; **18**: 978-986.
754 32. Zerbib F, Roman S, Bruley Des Varannes S*, et al.* Normal values of pharyngeal and
755 esophageal 24-hour pH impedance in individuals on and off therapy and interobserver
756 reproducibility. *Clin Gastroenterol Hepatol* 2013; **11**: 366-372.
757 33. Banasiuk M, Banaszkiewicz A, Dziekiewicz M, Zaleski A, Albrecht P. Values From
758 Three-dimensional High-resolution Anorectal Manometry Analysis of Children Without
759 Lower Gastrointestinal Symptoms. *Clinical gastroenterology and hepatology : the official*
760 *clinical practice journal of the American Gastroenterological Association* 2016; **14**: 993-
761 1000.e1003.
762 34. Lee HJ, Jung KW, Han S*, et al.* Normal values for high-resolution anorectal
763 manometry/topography in a healthy Korean population and the effects of gender and
764 body mass index. *Neurogastroenterol Motil* 2014; **26**: 529-537.

35. Li Y, Yang X, Xu C, Zhang Y, Zhang X. Normal values and pressure morphology for three-dimensional high-resolution anorectal manometry of asymptomatic adults: a study in 110 subjects. *International journal of colorectal disease* 2013; **28**: 1161-1168.
36. Sauter M, Heinrich H, Fox M*, et al.* Toward more accurate measurements of anorectal motor and sensory function in routine clinical practice: validation of high-resolution anorectal manometry and Rapid Barostat Bag measurements of rectal function. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society* 2014; **26**: 685-695.
37. Pandolfino JE. High-resolution manometry: is it better for detecting esophageal disease? *Gastroenterology & hepatology* 2010; **6**: 632-634.
38. Ratuapli S, Bharucha AE, Harvey D, Zinsmeister AR. Comparison of rectal balloon expulsion test in seated and left lateral positions. *Neurogastroenterol Motil* 2013; **25**: e813-820.
39. Thekkinkattil DK, Lim MK, Nicholls MJ, Sagar PM, Finan PJ, Burke DA. Contribution of posture to anorectal manometric measurements: are the measurements in left-lateral position physiologic? *Dis Colon Rectum* 2007; **50**: 2112-2119.
40. Grossi U, Carrington EV, Bharucha AE, Horrocks EJ, Scott SM, Knowles CH. Diagnostic accuracy study of anorectal manometry for diagnosis of dyssynergic defecation. *Gut* 2016; **65**: 447-455.
41. Ratuapli SK, Bharucha AE, Noelting J, Harvey DM, Zinsmeister AR. Phenotypic identification and classification of functional defecatory disorders using high-resolution anorectal manometry. *Gastroenterology* 2013; **144**: 314-322.e312.
42. Rao SSC, Kavlock R, Rao S. Influence of body position and stool characteristics on defecation in humans. *Am J Gastroenterol* 2006; **101**: 2790-2796.
43. Heinrich H, Reiner C, Parker H*, et al.* Seated evaluation of anorectal function by high resolution manometry: a randomized comparison of measurements in the seated and left lateral positions. *Gastroenterology* 2016; **150**: S176.
44. Emir H, Akman M, Sarimurat N, Kilic N, Erdogan E, Soylet Y. Anorectal manometry during the neonatal period: its specificity in the diagnosis of Hirschsprung's disease. *European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery [et al] = Zeitschrift fur Kinderchirurgie* 1999; **9**: 101-103.
45. De Lorijn F, Reitsma JB, Voskuijl WP*, et al.* Diagnosis of Hirschsprung's disease: a prospective, comparative accuracy study of common tests. *The Journal of pediatrics* 2005; **146**: 787-792.
46. Pehl C, Enck P, Franke A*, et al.* [Anorectal manometry]. *Zeitschrift für Gastroenterologie* 2007; **45**: 397-417.
47. Prott G, Hansen R, Badcock C, Kellow J, Malcolm A. What is the optimum methodology for the clinical measurement of resting anal sphincter pressure? *Neurogastroenterol Motil* 2005; **17**: 595-599.
48. McHugh SM, Diamant NE. Effect of age, gender, and parity on anal canal pressures. Contribution of impaired anal sphincter function to fecal incontinence. *Dig Dis Sci* 1987; **32**: 726-736.
49. Bielefeldt K, Enck P, Erckenbrecht JF. Sensory and motor function in the maintenance of anal continence. *Dis Colon Rectum* 1990; **33**: 674-678.
50. Deutekom M, Dobben AC, Terra MP*, et al.* Clinical presentation of fecal incontinence and anorectal function: what is the relationship? *Am J Gastroenterol* 2007; **102**: 351-361.

812 51. Felt-Bersma RJ, Klinkenberg-Knol EC, Meuwissen SG. Anorectal function
813 investigations in incontinent and continent patients. Differences and discriminatory
814 value. *Dis Colon Rectum* 1990; **33**: 479-485; discussion 485-476.
815 52. Fernandez-Fraga X, Azpiroz F, Malagelada JR. Significance of pelvic floor muscles
816 in anal incontinence. *Gastroenterology* 2002; **123**: 1441-1450.
817 53. Hiltunen KM. Anal manometric findings in patients with anal incontinence. *Dis*
818 *Colon Rectum* 1985; **28**: 925-928.
819 54. Holmberg A, Graf W, Osterberg A, Pahlman L. Anorectal manovolumetry in the
820 diagnosis of fecal incontinence. *Dis Colon Rectum* 1995; **38**: 502-508.
821 55. Pehl C, Seidl H, Scalercio N*, et al.* Accuracy of anorectal manometry in patients with
822 fecal incontinence. *Digestion* 2012; **86**: 78-85.
823 56. Rasmussen OO, Sorensen M, Tetzschner T, Christiansen J. Dynamic anal
824 manometry: physiological variations and pathophysiological findings in fecal
825 incontinence. *Gastroenterology* 1992; **103**: 103-113.
826 57. Bharucha AE, Fletcher JG, Harper CM*, et al.* Relationship between symptoms and
827 disordered continence mechanisms in women with idiopathic faecal incontinence. *Gut*
828 2005; **54**: 546-555.
829 58. Hill J, Corson RJ, Brandon H, Redford J, Faragher EB, Kiff ES. History and
830 examination in the assessment of patients with idiopathic fecal incontinence. *Dis Colon*
831 *Rectum* 1994; **37**: 473-477.
832 59. Engel AF, Kamm MA, Bartram CI, Nicholls RJ. Relationship of symptoms in faecal
833 incontinence to specific sphincter abnormalities. *Int J Colorectal Dis* 1995; **10**: 152-155.
834 60. Bordeianou L, Lee KY, Rockwood T*, et al.* Anal resting pressures at manometry
835 correlate with the Fecal Incontinence Severity Index and with presence of sphincter
836 defects on ultrasound. *Dis Colon Rectum* 2008; **51**: 1010-1014.
837 61. Wickramasinghe DP, Perera CS, Senanayake H, Samarasekera DN. Correlation of
838 three dimensional anorectal manometry and three dimensional endoanal ultrasound
839 findings in primi gravida: a cross sectional study. *BMC Res Notes* 2015; **8**: 387.
840 62. Bharucha AE, Rao SS. An update on anorectal disorders for gastroenterologists.
841 *Gastroenterology* 2014; **146**: 37-45.e32.
842 63. Pehl C, Enck P, Franke A*, et al.* [Anorectal manometry]. *Z Gastroenterol* 2007; **45**:
843 397-417.
844 64. Heinrich H, Sauter M, Fox M*, et al.* Assessment of Obstructive Defecation by High-
845 Resolution Anorectal Manometry Compared With Magnetic Resonance Defecography.
846 *Clin Gastroenterol Hepatol* 2015; **13**: 1310-1317.e1311.
847 65. Palit S, Thin N, Knowles CH, Lunniss PJ, Bharucha AE, Scott SM. Diagnostic
848 disagreement between tests of evacuatory function: a prospective study of 100
849 constipated patients. *Neurogastroenterol Motil* 2016; **28**: 1589-1598.
850 66. Kahrilas PJ, Bredenoord AJ, Fox M*, et al.* The Chicago Classification of esophageal
851 motility disorders, v3.0. *Neurogastroenterol Motil* 2015; **27**: 160-174.
852 67. Kahrilas P, Ghosh S, Pandolfino J. Esophageal motility disorders in terms of
853 pressure topography: the Chicago Classification. *J Clin Gastroenterol* 2008; **42**: 627-635.
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856 **TABLES**

857

858 **Table 1**. Frequency of respondents' location by country.

859

Country	Frequency	%
United Kingdom	29	27.1
United States	15	14
Mexico	11	10.3
Germany	8	7.5
Italy	5	4.7
Switzerland	5	4.7
Australia	4	3.7
Argentina	3	2.8
Chile	2	1.9
Ireland	2	1.9
Korea, Republic of	2	1.9
Malaysia	2	1.9
Spain	2	1.9
Colombia	1	0.9
Costa Rica	1	0.9
Ecuador	1	0.9
Egypt	1	0.9
France	1	0.9
Guatemala	1	0.9
India	1	0.9
Netherlands	1	0.9
Nicaragua	1	0.9
Poland	1	0.9
Russia	1	0.9
Singapore	1	0.9
South Africa	1	0.9
Sweden	1	0.9
Thailand	1	0.9
Turkey	1	0.9
United Arab Emirates	1	0.9
Total	**107**	**100**

860

Table 2. Frequency tables of channel number and distribution for (a) water-perfused and (b) solid-state catheter systems used by respondents.

(a)

Water perfused manometry: Number of water-perfused channels	**Frequency**	**%**
2 - 4	8	17
5 - 8	30	63.8
9 - 11	2	4.3
>12	6	12.8
I'm not sure	1	2.1
Total	47	100

Water perfused manometry: Arrangement of water-perfused channels	**Frequency**	**%**
Longitudinally	5	10.6
Spirally	25	53.2
Radially	12	25.5
Longitudinally and radially	4	8.5
I'm not sure	1	2.1
Total	47	100

(b)

Solid state manometry: Number of solid-state sensors	**Frequency**	**%**
1	1	1.7
2 - 4	11	18.6
5 - 8	7	11.9
9 - 12	18	30.5
13 - 20	2	3.4
21 - 40	4	6.8
>40	11	18.6
I'm not sure	5	8.5
Total	59	100

Solid state manometry: Arrangement of solid-state sensors	**Frequency**	**%**
Longitudinally	1	1.7
Spirally	15	25.4
Radially	8	13.6
Longitudinally and radially	29	49.2
I'm not sure	6	10.2
Total	59	100

Table 3. Frequency table of patient positioning during the push manoeuver.

Position during push manoeuver	Total N=89	
	n	%
Supine	5	5
Left Lateral	81	76
Sitting on a commode	11	10
Other	1	1

Table 4. Frequency tables showing use of additional investigations of anorectal function.

Associated investigations	Never		Sometimes		Always		Total
	n	%	n	%	n	%	n
Anal electromyography	92	85.9	13	12.1	2	1.9	107
Anal endosonography (endoanal ultrasound)	59	55.1	36	33.6	12	11.2	107
Anal sensation (electrical stimulation)	83	77.5	15	14	9	8.4	107
Balloon expulsion	26	24.3	23	21.5	58	54.2	107
Colonic scintigraphy	87	81.3	19	17.8	1	0.9	107
Colonic transit	21	19.7	47	43.9	39	36.4	107
Evacuation proctography	38	66.3	45	42.1	24	22.4	107
Pudendal nerve function (terminal motor latencies)	49	45.8	24	22.4	34	31.8	107
Rectal sensation (balloon distension)	52	48.6	7	6.5	48	44.9	107
Rectal sensation (electrical stimulation)	88	82.2	10	9.3	9	8.4	107
Rectal sensation / compliance (barostat)	88	82.2	9	8.4	10	9.3	107
Saline continence test	69	64.4	19	17.8	19	17.8	107

FIGURE LEGENDS

Figure 1: Table and diagram showing frequency of measurement parameters utilised for rest, squeeze, prolonged squeeze and cough during ARM protocols.

Figure 2: Comparative histograms of (a) squeeze and (b) prolonged squeeze showing maneuver duration reported during ARM protocols.

Figure 3: Comparative histograms of (a) squeeze, (b) prolonged squeeze, (c) push and (d) RAIR showing number of maneuvers performed during ARM protocols.